Mount Hood 2023 Challenges

(Type 2 Diabetes)

Motivation:

The impact of model uncertainty on cost-effectiveness estimates of diabetes interventions is unknown. The aim of the Mt Hood 2023 challenges is to replicate the Mt Hood 2022 costeffectiveness challenge set for a generic "Asian" Population. We recognise there is substantial intra-regional variation in population characteristics, potential responsiveness to treatment, and the costs and utilities attributed to diabetes and complication events. Nevertheless this challenge represents a step towards understanding the variability in model cost-effectiveness estimates within this region. This challenge examines the variation in cost-effectiveness estimates associated with two categories of diabetes interventions: a

reduction in a patient's blood glucose levels and a reduction in weight. Model estimates will be used to understand the impact of model uncertainty within this population.

To aid reporting, please note the information requested in the preliminary Excel Tabs. For this challenge we have included an additional request for information on how ethnicity affects outcomes in your model within the Excel tab "Model Description".

Challenge 1: Revisiting the reference simulation

We will first ask groups to repeat the reference simulations for a standard patient that were in previous challenges and reported in the MT Hood model registry. This will enable model simulations to be compared across time and region. These values will be used to update the model registry: https://www.mthooddiabeteschallenge.com/registry. Previous reference simulations have often assumed that risk factors are held constant over time which is often unrealistic. Since the 2018 Mt Hood challenge several risk factor time path equations have been published (eg https://onlinelibrary.wiley.com/doi/10.1111/dme.14656). Hence we ask all modelling groups to run the reference simulations under two scenarios: (i) risk factor values held constant (which was the assumption from the previous challenge); and (ii) allowing them to vary using equations or trajectories that are normally used in your simulation model. Treatment effects will assume to be a constant displacement from the usual time path.

Challenge: Simulating costs and cost-effectiveness

Following the 2022 and 2018 Mt Hood Quality of life Challenge, the challenge employs average values or characteristics of patients enrolled in RCTs of common diabetes therapies. The average treatment effect of each category of intervention will be modelled by permanent reduction in HbA1c and body mass index. The results from this exercise will provide an indication of what factors influence the cost-effectiveness of these interventions. The challenge will also examine how the estimated incremental QALYs, incremental costs and ICERs vary for a cohort of patients with a history of myocardial infarction and following the inclusion of unrelated future medical costs.

Model Inputs:

Utility Values

The challenge uses health utility values for type 2 diabetes representative of an east and south-east Asian population (Table 1). It will be adequate to use point estimates and not model second order uncertainty if the model allows it. As a reminder, given utility *decrements* are presented in table 1 for all events apart from the baseline utility, 95% confidence intervals may be inverted from their presentation here in your model implementation. We report the most extreme disutility as the lower 95% CI, but model implementation may differ.

If possible, please set utility weights to zero for any health states where utilities are not reported in table 1. If this is not possible, and you require real utility weights for additional health states not listed, please add utility values you currently use. Please document your sources and assumptions in the "Utility values" tab in the accompanying Excel spreadsheet.

For the challenge, please apply disutility values only to complication events described in the instructions as far as possible. If this is not possible and your model **requires** you to apply additional disutilities for certain health states (e.g. a raised BMI health state which is independent of BMI's effect on complication events) - please report these disutilities here. Please also keep baseline utilities constant across all ages as set out in instruction table 1. Where possible, please do not change baseline utilities by age. However, if your model requires you to do so – please report this in the Excel sheet.

Note: please make sure to avoid confusion with utility/disutility terminology in loading the models and in reporting results. The "Utility/Disutility Values" column in Table 1 reports "utility" only for diabetes without complication (which is positive). The remaining items (all negative) are disutility and are incremental.

Based on the 2018 Mt. Hood challenge conference call on September 5, 2018, two suggestions were made for the Quality of Life challenge, including:

1) The additive quality-of-life (QoL) model is recommended when populating the health utility values into the simulation model. As shown in Table 1 below, if a subject has experienced two different complications belonging to 2 different categories of disease (e.g., stroke [in the category of cerebrovascular disease] and myocardial infarction [in the category of coronary heart disease]), the health utility value will be reduced by 0.219 which is the sum of individual decrement for these 2 complications (i.e., 0.164+0.055). However, if a subject has experienced two or more complications within the same category of disease (e.g., myocardial infarction [in the category of coronary heart disease] and congestive heart failure [in the category of coronary heart disease]), the health utility value will be reduced by 0.108 (the decrement for heart failure) which is the largest decrement of these two complications. If the additive QoL model is not feasible in your model, please document your assumptions how the health utility values are populated in your model.

2) The utility decrement and its 95% confidence interval for renal transplant was assumed to be half of those for hemodialysis. In this instance, utility values for Hemodialysis *(italicized)* were imputed accordingly from utilities available for renal transplant.

Table 1. Utility values by categories of diseases/complications

Disease category	Complication level provided in Mt. Hood QoL challenge	Type 2 diabetes [a]		
		Utility/Disutility Values	Lower 95% CI	Upper 95% CI
Baseline utility value	Diabetes without complications	0.881	0.833	0.929
	Major hypoglycemia event	-0.028	-0.048	-0.009
	Major hyperglycemic event	0	0	0
Comorbidity	Excess BMI (each unit above 23 kg/m^2)	-0.002	-0.020	0.017
Diabetic Eye Disease	Cataract	-0.016	-0.031	-0.001
	Moderate non-proliferative background diabetic retinopathy	0	0	0
	Vision-threatening diabetic retinopathy	-0.023	-0.034	-0.011
	Severe vision loss	-0.101	-0.143	-0.059
Nephropathy	Proteinuria	-0.022	-0.037	-0.007
	Renal transplant	-0.053	-0.081	-0.025
	Hemodialysis	*-0.106*	*-0.162*	*-0.050*
	Peripheral vascular disease	-0.017	-0.125	-0.090
Neuropathy	Neuropathy	-0.052	-0.064	-0.041
	Active ulcer	0	0	0
	Amputation event	-0.177	-0.291	-0.063
Cerebrovascular disease	Stroke	-0.086	-0.112	-0.060
Cardiac disease	Myocardial infarction	-0.007	-0.036	-0.022
	Ischemic heart disease	-0.017	-0.041	-0.007
	Heart failure	-0.050	-0.081	-0.020
	Percutaneous revascularization	0	0	0
	Coronary revascularization	0	0	0

Source: [a] Mok C H, Kwok H H.Y. Ng C S, Leung G M, Quan J Health State Utility Values for Type 2 Diabetes and Related Complications in East and Southeast Asia: A Systematic Review and Meta-Analysis. Value in Health 2021

0s represent that no utility value has been sourced for these parameters. Please set these (and any additional) events to have zero impact on calculated utility where possible to maintain comparability between model results. If not possible to use a zero value, please document your default utility assumption in the Excel submission file.

Patient Baseline Characteristics

To allow for consistent comparisons across all models, baseline patient characteristics should follow the values as listed in Table 2. If more specific ethnicity categories are available within the simulation model, please select an ethnicity which best matches the "East and South East Asian" ethnicity used for calculation of utilities. In all instances, please report the ethnic population named in your model for which your results are derived. Any other baseline patient characteristics that your model may require can be sourced from publicly available literature (but please document this including sources in "Baseline Characteristics" tab in the accompanying Excel spreadsheet).

Table 2: Patient Baseline Characteristics

Patient Characteristics	**Type 2 diabetes [a]**	
	Men	**Women**
Current age	65	65
Duration of diabetes	8	8
Current/former smoker	N	N
Ethnicity	"Asian"	"Asian"
HbA1c %	7.7	7.7
Systolic Blood Pressure, mmHg	141	141
Diastolic Blood Pressure, mmHg	79	79
Total Cholesterol, mmol/l	5.2	5.2
HDL Cholesterol, mmol/l	1.3	1.3
LDL Cholesterol, mmol/l	3.2	3.2
Triglycerides, mmol/L	1.6	1.6
BMI	23	23
Albumin: creatinine ratio (mg/g)	18.0	18.0
Peripheral Vascular Disease (PVD)	N	N
Micro or macro albuminuria (albuminuria >50 mg/g)	N	N
Atrial fibrillation	N	N
eGFR (ml/min/1.73 m2)	77 [b]	77 [b]
Prior history of macrovascular disease	N	N
Prior history of microvascular disease	N	N

Source: [a] Does Glycemic Control Offer Similar Benefits Among Patients With Diabetes in Different Regions of the World?: Results from the ADVANCE trial. [b] Survival of Chinese people with type 2 diabetes and diabetic kidney disease: a cohort of 12 -year follow-up.

Costs

The perspective of the cost analysis is a representative "Asian" health care system – in this case healthcare costs in mainland China. Table 3 shows mean complication costs of diabetic patients. These costs were retrieved from studies published between Jan 1, 2018 to Sep 16, 2021, however these costs have not been indexed to a particular cost year. Please apply the same set of complication costs for both men and women and for type 2 diabetes individuals.

Please apply costs only to complication events described in the instructions as far as possible. To give example, if your model usually incorporates increased costs from raised BMI increases independently of complication events which occur, please turn this off, if possible. If not possible to model costs only for complication events, then please report any additional costs separately.

Additionally, please keep baseline costs in the absence of complications constant across all ages as set out in instruction table 3. Please use zero values for all additional cost elements your model may include beyond those listed in table 3, where possible. However, if your model does not permit this – please report values used in the excel spreadsheet.

Table 3 Complication costs (US $)

	Year of Event	**Cost in subsequent years**
Diabetes in absence of complications	,414	
Myocardial Infarction	9,804	6,623
Ischaemic Heart Disease	5,530	4,817
Heart Failure	5,194	6,262
Cerebrovascular Disease	4,091	5,357
Peripheral Vascular Disease	4,246	4,806
Neuropathy	3,643	4,612
Amputation	5,932	)
Renal Failure	2,653	3,804

Cataract	1,556	0
Retinopathy	3,971	4,858
Haemodialysis	11,775	20,027

Source: Jianchao Quan, Zhenping Zhao, Limin Wang, Carmen S. Ng, Harley H.Y. Kwok, Mei Zhang, Sunyue Zhou, Jiaxi Ye, Xin Jiong Ong, Robyn Ma, Gabriel M. Leung, Karen Eggleston, Maigeng Zhou. Potential health and economic impact associated with achieving risk factor control in Chinese adults with diabetes: a microsimulation modelling study. The Lancet Regional Health - Western Pacific. 2023. https://doi.org/10.1016/j.lanwpc.2023.100690

0s represent that no cost value has been sourced for these parameters. Please set these (and any additional) events to have zero impact on calculated costs where possible to maintain comparability between model results. If not possible to use a zero value, please document your default cost assumption in the Excel submission file

Table 4 Mean Intervention effect costs (US $) (assume applied every year while patients are alive in the simulation)

Intervention	Mean effect	Mean annual cost ($)
Blood glucose intervention 1:	0.5% point reduction in HbA1c & no effect on BMI	280
Blood glucose intervention 2:	0.9% point reduction in HbA1c &) 1-unit **increase** in BMI (kg/m2)	415
Blood glucose intervention 3:	1.5% point reduction in HbA1c & 1-unit **reduction** in BMI (kg/m2)	1,866

Challenge simulation

Step 1: Run a simulation using the baseline risk factors from Table 2 held constant over a 40-year period for type 2 diabetes, separately for males and for females

This simulation should match both the 2018 Mt Hood challenge and the reference case simulations which are on the Mt Hood website: (https://www.mthooddiabeteschallenge.com/refsim). Ensure the costs and health outcomes are **not discounted** for this challenge.

Extract the results and enter input values in a transparent manner in the accompanying Excel workbook in tab labelled "Time paths & Outcomes" (modify the workbook to fit your outcomes if necessary, but please try to preserve the basic structure). Do not forget to include traces (risk factor time paths) for input values of all the above risk factors; rates (or counts) of all major health states in the model (e.g. MI; stroke; renal failure, etc.), and life-expectancy.

For microsimulation models, please ensure that the number of replications is sufficient to generate stable results.

Step 2: Reference simulation of common treatment effects

Re-run the simulation with four individual interventions (one-at-a-time and then all combined), separately for males and females, that capture initial and permanent reductions in common risk factors from time paths modelled in Step 1. Reductions from these interventions should only be applied to post-baseline cycles and baseline values should remain unchanged.

(i) 0.5%-point reduction in HbA1c;
(ii) 10mm Hg reduction in Systolic Blood Pressure;
(iii) 0.5 mmol/l (19.33 mg/dl) reduction in LDL Cholesterol
(iv) 1-unit reduction in BMI (kg/m2)
(v) All 4 of the interventions above applied simultaneously#

Extract the results and add to the accompanying Excel workbook (in tab labelled "Time paths & Outcomes". Report outcomes and inputs in a transparent manner. Do not forget to include traces (numerical or curves) for input values of all the above risk factors; cumulative rates (or counts) of all major health states in the model (e.g. MI; stroke; renal failure, etc.) and life expectancy.

Step 3: Estimate incremental QALYs, separately for males and females

Using the "Utility/disutility" values in Table 1 run the baseline simulation and estimate expected QALYs, assuming that decrements apply to the year of the of the event and are similarly applied to each subsequent year. However, if temporary events/states such as hypoglycaemia are modelled, it is likely that these decrements only apply to the year of the event. If so, please document this.

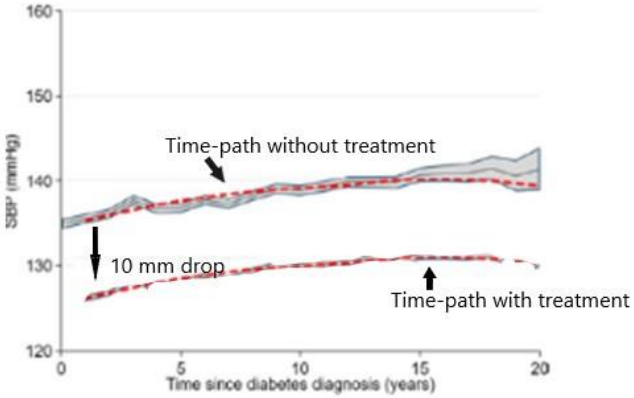
Run each of the four interventions listed in Step 2 to estimate the expected QALYs and calculate the incremental QALYs compared to the baseline (control). Extract the results and add to the accompanying Excel workbook (in tab labelled "Time paths & Outcomes").

Be sure to report incremental QALYs so that a negative value indicates worse QALYs (not inverting to account for a positive value indicating more disutility)

Step 4: Reference simulation of common treatment effects when risk-factor timepaths are NOT held constant

The simulation in step 1 does not capture the drift that can occur in many risk factors over time eg. the gradual increase in HbA1c. To understand what impact change in risk factors may have on incremental benefits the second component of this challenge is to redo the four simulations outlined in step 2 using the actual risk factor time paths or assumptions regularly used in your model. Please assume that treatment effects are permanent vertical displacements from the trajectories without intervention timepaths.

As an example consider the blood pressure treatment simulation – the treatment will permanently reduce SBP 10 mm Hg below the projected trajectory of SPB without treatment. Similarly, please allow all risk factors that are normally projected in your model to vary. So, when simulating the blood pressure lowering intervention allow HbA1c, LDL, BMI and other risk factors to follow the time-path predicted by your model without any treatment effect.



Extract the results and add to the accompanying Excel workbook (in tab labelled “Time paths & Outcomes”. Report outcomes and inputs in a transparent manner. Do not forget to include traces (numerical or curves) for input values of all the above risk factors; cumulative rates (or counts) of all major health states in the model (e.g. MI; stroke; renal failure, etc.), QALYs and life expectancy.

Challenge 2: Simulating costs and cost-effectiveness of hypothetical interventions

Challenge two involves a cost-effectiveness evaluation on a hypothetical cohort of the male and female patients that have been simulated in the first challenge. For this challenge assume that there are equal numbers of females & males. Groups are asked to report overall cost-effectiveness results for the cohort in the remaining challenges.

Step 5: Simulate three glucose lowering interventions

Re-run the simulation with three hypothetical interventions affecting blood glucose and BMI that capture initial and permanent reductions in common risk factors from time paths modelled in Step 1. Table 4 presents the effects of the interventions and respective annual costs.

It is important in each simulation that all risk factors are kept constant between simulations and limit variation to the intervention effects and costs as per instructions in the steps below. This includes assumptions around biomarker evolution; i.e. HbA1c and BMI should be kept constant over time and not allowed to change over time (i.e., drift).

Please apply the same effect and annual costs for both men and women over the whole simulation period. These costs are unchanged by the occurrence of complications. Assume that the interventions will not have an effect on any other risk factors than HbA1c and BMI. Finally, assume adherence to each intervention to be 100% during the whole simulation period. Although the interventions are hypothetical, their effect size is based on a meta-analysis of glycaemic drugs [https://ascpt.onlinelibrary.wiley.com/doi/epdf/10.1002/cpt.1307] and their costs from regional publications reporting Chinese national insurance drug prices in 2021 [https://doi.org/10.3389%2Ffendo.2021.684960] & [https://doi.org/10.3389/fpubh.2023.1201818].

To estimate QALYs, use the utility values from Table 1 and follow the same assumptions as in Step 3. Estimate non-intervention costs (complications and management) by applying the costs from Table 3. Document any additional health states and/or costs used beyond those in Table 3.

The main outputs required are:

- incremental QALYs,
- incremental costs and
- incremental cost-effectiveness ratios

Report the above for the overall cohort of 50:50 males/females Conduct these simulations from an "Asian" perspective, using and reporting costs in US dollars ($) and **setting the discount rate to 3.5%** for QALYs and costs prior to running the simulations.

Please use the minimum number of loops to reach convergence for the main outputs of interest. Report the number of loops used in each simulation.

Extract the results and add to the accompanying Excel workbook (in tab labelled "costs & ICERs"). Do not forget to include traces (numerical or curves) for input values of HbA1c and BMI risk factors.

Be sure to report incremental QALYs and costs of each intervention relative to no intervention so that a negative value indicates worse QALYs for the intervention compared to no intervention (not inverting to account for a positive value indicating more disutility)

Step 6: Estimate incremental QALYs and incremental costs for patients with a history of myocardial infarction (optional)

Re-run the simulation for a cohort of patients with a history of prior myocardial infarction again using the mean intervention costs provided in Table 4. If your model requires a number of years since the event, please use 5 years for all patients. Re-run for each of the blood glucose interventions, estimate the expected incremental QALYs and incremental costs, and calculate ICERs for each intervention compared to no intervention. Extract the results and add to the accompanying Excel workbook (in tabs labelled "Costs & ICERs").

Summary of findings:

Compile a summary of your findings in the accompanying Excel spreadsheet (in tab labelled "Summary"). Please complete the following.

A) Based on your results in Step 5, which intervention(s) were costs-effective at a $12,618 per QALY* threshold?
B) Based on your results in Step 6, report which intervention(s) were costs-effective at a $12,618 per QALY* threshold?
C) Provide an overview of what you learnt from this challenge.

* China GDP per capita in 2021 reported by the World Bank: https://data.worldbank.org/indicator/NY.GDP.PCAP.CD?locations=CN

Submission:

Prior to the meeting, please submit the Excel spreadsheet ("MH MALAYSIA CHALLENGE – ICER challenge_GROUP") to Mount Hood at: mthood2016@gmail.com **by 24th of November 2023.** Please replace GROUP with your modelling group name before submission.